

REMARKS

This amendment and remarks are in response to the Office Action of February 24, 2006. Claims 1 and 3-11 and 13 were in the case. New Claims 15-20 are added and find their support in the Markush definitions of R<sup>4</sup> and the examples in the specification. New Claims 21-40 are added from provisional filing 60/419,791 and amended according to the restriction requirement provided in this case.

**35 U.S.C. § 112**

Claims 1 and 3-10 stand rejected as lacking enablement. Applicants note that the Office acknowledges the enablement of the species of Claim 11. Accordingly, the remaining issue is the enablement of the nonexemplified species.

**The Federal Circuit answered this question in *In re Angstadt*.**

“The question, then, is whether in an unpredictable art, section 112 requires disclosure of a test with every species covered by a claim. To require such a complete disclosure would apparently necessitate a patent application or applications with "thousands" of examples . . . along with information as to whether each exhibits [the claimed utility]. More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. **This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments, which are expressly disclosed.** A potential infringer could readily avoid "literal" infringement of such claims by merely finding another analogous [compound], which could be used in [the utility].

Having decided that appellants are not required to disclose every species encompassed by their claims even in an unpredictable art such as the present record presents, each case must be determined on its own facts. In the instant [\*\*12] case, appellants' invention is the use of a complex catalyst comprising a hexaalkylphosphoramidate and a transition metal salt to catalyze the oxidation of secondary or tertiary alkylaromatic hydrocarbons to form hydroperoxides. Appellants have, in effect, provided those skilled in this art with a large but finite list of transition metal salts from which to choose in preparing such a complex catalyst. Appellants have actually carried out 40 runs using various transition metal salts and hexaalkylphosphoramidates. **If one skilled in this art wished to make and use a transition metal salt other than those disclosed in appellants' 40 runs, he would merely read appellants' specification for directions how to make and use**

**the catalyst complex to oxidize the alkylaromatic hydrocarbons, and could then determine whether hydroperoxides are, in fact, formed.** The process discovered by appellants is not complicated, and there is no indication that special equipment or unusual reaction conditions must be provided when practicing the invention. . . . Thus, we have no basis for concluding that persons skilled in this art, armed with the specification and its 40 working examples, would not easily be able to determine which catalyst complexes within the scope of the claims work to produce hydroperoxides and which do not.

Since appellants have supplied the list of catalysts and have taught how to make and how to use them, we believe that the experimentation required to determine which catalysts will produce hydroperoxides would not be undue and certainly would not "require ingenuity beyond that to be expected of one of ordinary skill in the art."

In re Angstadt, 537 F.2d 498, 503 (C.C.P.A. 1976)

The specification contains 287 examples and a generic scheme (p. 54) to allow one of ordinary skill to make the full scope of the claimed compounds. The Applicants have provided several common assays with which to test the activity of the remaining compounds. Accordingly, in light of In re Angstadt, the unexemplified claimed compounds are enabled.

Applicants also submit that the rejection of the pending claims for being unenabled with regard to their use is improper under MPEP 2164.01(c). This provision states that where the specification contains a connotation of how to use the compounds, enablement is satisfied. Moreover, where the compound claim is not limited by a recited use, as is the case, any use that would reasonably correlate to the scope of the claim precludes a rejection for nonenablement of that claim. While the Office Action speculates as to the activity of unexemplified compounds, the Office has failed to show why it would be unreasonable for the claimed compounds to be useful for the stated utility as required by 2164.01(c).

The Office holds that the claimed compounds are not enabled as to their use because the Office does not believe there is a reasonable basis for assuming that the nonexemplified claimed compounds share the physiological properties needed to practice the invention. There is no dispute as to the usefulness of the exemplified

species within the claims. However, MPEP 2164.02 states that proof of enablement for nonexemplified members of the claimed genus is required only where the Office establishes that a person skilled in the art could not use the genus as a whole without undue experimentation.

One of skill in the art can look to the specification including the 287 examples to see how the claimed heteroaryl-piperazine-benzimidazoles and -imidazopyridines can be made. The specification also discloses formulation information and modes of deliver. The only experimentation remaining for one of skill in the art is to run the unexemplified compound through one of the disclosed assays. Applicants request clarification as to what undue experimentation is required given this disclosure.

An analysis of all of the Wands factors leads one to the same conclusions as above. The factors to be considered are (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

**(1) The Quantity of Experimentation Necessary**

Applicants have disclosed a generic method and 287 specific examples useful for making the compounds within the scope of the claims. Therefore, the experimentation required is limited to running a standard cell-based assay, as present in the specification as filed. This skill is common for anyone working in the pharmaceutical arts.

**(2) The Amount of Direction or Guidance Presented**

The specification provides 287 examples as guidance along with a generic method teaching. Additionally, the specification lists several different assays that can be used to verify activity of the claimed compounds. According to In re Angstadt, sufficient direction and guidance is provided. The specification also lists formulation examples and methods of administration.

**(3) The Presence or Absence of Working Examples**

The specification as filed contained 287 examples of compounds having the specified utility.

**(4) The Nature of the Invention**

The nature of the invention is a set of novel pharmaceutical compounds useful for the stated utility.

**(5) The State of the Prior Art**

Compounds of this nature were not previously known as VR1 antagonists. However, the prior art teaches general methods of running assays, etc.

**(6) The Relative Skill of Those in the Art**

A research associate in the pharmaceutical industry. Relatively high.

**(7) The Predictability or Unpredictability of the Art**

As the court in *Angstadt* noted, even in unpredictable arts, exemplification of every species is not necessary. Unpredictability in this case is minimal given the plethora of examples provided in the specification.

**(8) The Breadth of the Claims**

The pending claims have been amended to include heteroaryl-piperazine-benzimidazoles and -imidazopyridines. Various other substituents are allowed around this three-ring core. Accordingly, Applicants believe that the pending claims are average in scope when compared to typical issued compound claims. Speculation as to the exact number of species able to fit within the claims is not relevant as that number varies case by case depending on the status of the art and the number of examples provided.

The key to this analysis is that the only experimentation required to enable the full scope of the claimed invention is that one of skill in the art would run a standard cell-based assay on analogues of exemplified compounds. The Office has not yet shown why the running of this assay would be considered undue experimentation. Accordingly, the Applicants believe the pending claims are enabled and ask for reconsideration of the pending rejection.

In order to advance prosecution, the Applicants have amended the Claims. Prompt reconsideration of the enablement rejection is respectfully requested.

**35 U.S.C. § 102(e)**

Claims 1, 3, 4 and 7-10 stand rejected as being anticipated by Sun. The 102(e) date for Sun is December 24, 2002. The Office Action refuses to recognize the priority date for the pending application of October 17, 2002 because the scope of four of the many variables in the claims differs.

There is no requirement that provisional application 60/419,791 describe exactly the subject matter claimed, but only sufficient information to clearly allow persons of ordinary skill in the art to recognize that the inventor actually invented what was claimed. *See In re Lukach*, 442 F.2d 967, 969, 169 U.S.P.Q. 795, 796 (C.C.P.A. 1971). Appellants believe that provisional application 60/419,791 supplies such sufficient information as is required.

Specifically, the following is a comparison of the definitions between the provisional and pending application:

**R<sup>c</sup>**

Pending Claim 1 R <sup>c</sup> is independently at each instance a saturated, <b>partially saturated</b> or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2, 3 or 4 atoms selected from N, O and S, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups;	Claim 2 of '791 R <sup>c</sup> is independently at each instance a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2, 3 or 4 atoms selected from N, O and S, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups;
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The insertion of the phrase partially saturated was to clarify that "saturated or unsaturated" included intermediate amounts of saturation, as one of skill in the art would understand.

**R<sup>5</sup> (and R<sup>5'</sup> as '791 used the same definition for both)**

The difference between the pending claims and the '791 application relates to R<sup>5</sup> being a substituted alkyl. However, both the pending claims and the '791 application allow for substituted alkyls. The Applicants merely brought the '791 definition of R<sup>d</sup> into the R<sup>5</sup> and R<sup>5'</sup> definitions in the pending claims for ease of prosecution.

**R<sup>c</sup> and R<sup>h</sup>**

R<sup>c</sup> was in the '791 application and R<sup>h</sup> is merely a shorthand reference to a group that can be H or Re.

Applicants realize that the pending claims are not verbatim copies of the '791 claims, however, this is not required for priority. While the look of the claims differs,

the invention is the same. The Office has not pointed to any substantive difference in the coverage between the priority claims and the pending claim, but is merely relying on the premise that they "do not appear to be co-extensive." Applicants respectfully request that the Office detail what subject matter they believe that is in the pending claims that was evidenced at the time of the priority filing.

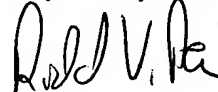
Applicants respectfully request that this rejection be withdrawn. Additionally, Applicants have added Claims 21-40, which come directly out of provisional application 60/419,791, which has been incorporated into this application by reference. Accordingly, these new claims have priority over Sun.

**35 U.S.C. § 103(a)**

Claims 5, 6 and 11 stand rejected as being obvious in light of Sun. The 102(e) date for Sun is December 24, 2002. The Office Action refuses to recognize the priority date for the pending application of October 17, 2002 because the scope of four of the many variables in the claims differs. Please see the above arguments. Also please note new Claims 21-40, which come out of the '791 priority application.

Applicants' attorney sincerely and respectfully requests that the Examiner consider, a telephone (805-447-3299) or personal interview to resolve any outstanding issues deemed appropriate by the Examiner.

Respectfully submitted,



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